other antibody is chosen from the group consisting of MAb 528 and antibodies which competitively inhibit the binding of MAb 528 to ErbB1.

Amend Claim 11 to read:

11. The assay of Claim 9 wherein the patient biological sample is chosen from the group consisting of blood, serum and plasma.

REMARKS

The Examiner rejected claims 9 and 12-23 on the basis that the specification was not enabling for detection of soluble ErbB1 in all biological samples. Claim 9, as amended, clarifies that the invention can be used to detect both soluble and other forms of ErbB1 in biological samples.

The Examiner further rejected claims 9-17 as being unpatentable over Harvey et al., U.S. patent 6,674,753, 1997, Partanen et al. (J. Occup. Med., 1994, vol. 36 pp 1324-1328) or Witters et al. (Clin. Cancer Res., 1995, vol. 1, pp. 551-557) in view of Graus-Porta et al. or Olayioye et al., and further in view of WO 94/11734 (Johansen et al., 1994).

Partanen et al., Witters et al., and Harvey '753 teach the detection of soluble EGFR forms in serum, urine, blood and plasma of cancer patients and teach that increased sEGFR concentrations are associated with disease, and in particular, cancer. In contrast, Applicants'invention teaches that decreased sEGFR concentrations are associated with cancer. Because EGFR is overexpressed in many human cancers and proteolytic cleavage has been believed to release soluble EGFR molecules from the plasma membrane of such tumors, the teachings of the present invention that serum sEGFR concentrations are lower in cancer patients

is not obvious. In addition, the immunoassays taught by Partanen et al. and patent '753 which use different antibodies toward EGFR and processes give disparate results for serum sEGFR concentrations compared to those of the present invention. In particular, Baron et al. (J. Immunol. Methods, 1998, vol. 219, pp. 23-43) and Baron et al. (Cancer Epidemiol. Biomark. Prev., 2001, vol. 10, pp. 1175-1185) compared to the immunoassays reported by Partanen et al. and patent '753 and noted that Applicants' invention has a greater dynamic range of serum sEGFR concentrations in human serum and thus has a superior ability or sensitivity to discern healthy subjects from cancer patients. The immunoassay of the present invention thereby fulfills a long-felt need in the field for an immunoassay having the operational characteristics to test whether sEGFR has utility in the risk assessment, screening, diagnosis, and prognosis of human cancer.

In short, one of ordinary skill would not know that decreased sEGFR concentrations were useful, and that the combination of matter, chemistry, and process (microtiter plates with covalent-linkage, antibodies, buffers, and acridinium-based photochemistry) described by the present invention would yield an immunoassay with unexpectedly superior properties with utility.

The Examiner noted that none of the first three references use the antibodies used by Applicants nor do they use the assay technique used by Applicants. The Examiner further notes that neither Graus-Porta nor Olayioye teach the assay method used by Applicants. Although Graus-Porta and Olayioye teach that two anti-EGFR antibodies, i.e., ERFR1 and 528, can be used for combined immunoprecipitation and immunoblotting purposes, they do not teach that these antibodies can be used to quantify EGFR or soluble ErbB1 in any context, let alone in human body fluids using sandwich-type microtiter plate-based immunoassays

Finally, Johansen does not teach direct labeling with acridinium nor the detection of the EGF receptor. Johansen teaches that chemiluminescent probes, such as acridinium esters, can be used to label avidin/streptavidin complexes in magnetic particle-basesd immunoassays, but does not teach that acridinium esters can be used to directly label any antibodies, and more specifically do not teach labeling antibodies that are specific for AGFR/ErbB1 (including antibody 528). Moreover, it is not obvious from Johansen that such acridinium-labeled antibodies would retain their bioactivity such that they could support microtiter plate-based immunoassays. In short, because one skilled in the art would not have thought to use an acridinium-coupled anti-EGFR antibodies, particularly acridinium-labeled antibody 528, to measure ErbB1 in human body fluids. Because the references do not use the assay technique described by Applicants, it would not have been obvious to combine the teachings of the three sets of disclosures. Nothing in any of the cited references suggest or teach such a combination and in fact such references teach away from such a combination, e.g., measurement of increased ErbB1 versus Applicants' invention which teaches measurement of decreased ErbB1.

CONCLUSION

Applicants respectfully submit that the present invention is not obviated by the teachings and that the patent application and claims therein, as amended, are in a condition for allowance. Reconsideration is, therefore, respectfully requested.

Respectfully submitted,

By: _____

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